

APPLICANT: C. Meese et al.
U.S.S.N.: Not Yet Assigned
[Continuation of USSN 09/700,094]
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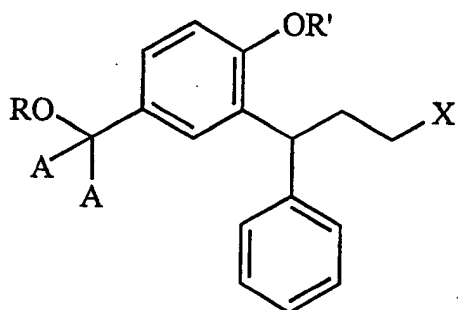
REMARKS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims:

Claims 1-27 (cancelled).

Claim 28 (new): A 3,3-Diphenylpropylamine of the formula I:



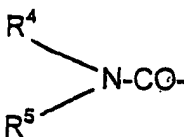
Formula I

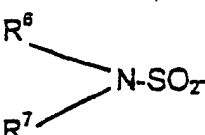
wherein R and R' are independently

- a) hydrogen, C₁-C₆ alkyl, C₃-C₁₀ cycloalkyl, substituted or unsubstituted benzyl, allyl or carbohydrate;
- b) C₁-C₆ alkoxy carbonyl, substituted or unsubstituted aryloxy carbonyl, benzoylacyl, benzoylglycyl, a substituted or unsubstituted amino acid residue;

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- c)  wherein R⁴ and R⁵ independently represent hydrogen, C₁-C₆ alkyl, substituted or unsubstituted aryl, benzyl or phenoxyalkyl wherein the alkyl residue has 1 to 4 carbon atoms or R⁴ and R⁵ form a ring together with the amine nitrogen;

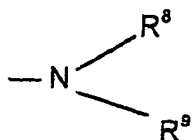
- d)  wherein R⁶ and R⁷ independently represent C₁-C₆ alkyl, substituted or unsubstituted aryl, benzyl or phenoxyalkyl wherein the alkyl residue has 1 to 6 carbon atoms;

- e) an ester moiety of inorganic acids, or

- f) -SiR_aR_bR_c, wherein R_a, R_b, R_c are independently C₁-C₄ alkyl or aryl,

with the proviso that at least one of R' and R is not hydrogen, and the proviso that R' is not methyl or benzyl when R is hydrogen, and R is not ethyl when R' is hydrogen,

X represents a tertiary amino group of formula Ia



Formula Ia

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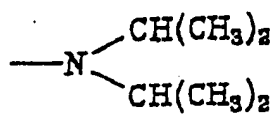
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wherein R⁸ and R⁹ represent C₁-C₆ alkyl groups, which may be the same or different and which together contain at least three carbon atoms, or R⁸ and R⁹ may form a ring together with the amine nitrogen,

A represents hydrogen (¹H) or deuterium (²H), and

their salts with physiologically acceptable acids, their free bases and, when the compounds are in the form of optical isomers, the racemic mixture and the individual enantiomers.

Claim 29 (new): The 3,3-Diphenylpropylamine as claimed in claim 28, wherein X is



Claim 30 (new): The 3,3-Diphenylpropylamine as claimed in claim 29 selected from:

(±)-2-acetamidoacetic acid 2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenyl ester,

(±)-malonic acid bis-[2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenyl] ester,

(±)-succinic acid bis-[2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethyl-phenyl] ester,

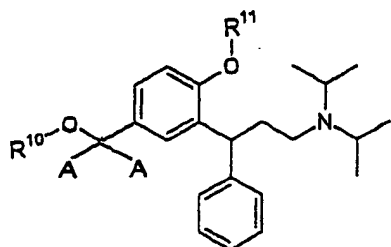
(±)-pentanedioic acid bis-[2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethyl-phenyl] ester,

(±)-hexanedioic acid bis-[2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenyl] ester.

Claim 31 (new): A 3,3-Diphenylpropylamine of the formula VI:

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Formula VI

wherein A represents hydrogen (^1H) or deuterium (^2H), and

their salts with physiologically acceptable acids, their free bases and, when the compounds are in the form of optical isomers, the racemic mixture and the individual enantiomers, and

wherein one of R^{10} and R^{11} is selected from $\text{C}_1\text{-C}_6$ alkyl, benzyl, alkoxy carbonyl, $\text{C}(\text{O})\text{NR}^4\text{R}^5$ and $-\text{SiR}_a\text{R}_b\text{R}_c$ and the other of R^{10} and R^{11} represents hydrogen.

Claim 32 (new): The 3,3-Diphenylpropylamine as claimed in claim 31 selected from the group consisting of:

- (\pm)-2-(3-diisopropylamino-1-phenylpropyl)-4-methoxymethyl-phenol,
- (\pm)-2-(3-diisopropylamino-1-phenylpropyl)-4-ethoxymethyl-phenol,
- (\pm)-2-(3-diisopropylamino-1-phenylpropyl)-4-propoxymethyl-phenol,
- (\pm)-2-(3-diisopropylamino-1-phenylpropyl)-4-isopropoxy-methylphenol,
- (\pm)-2-(3-diisopropylamino-1-phenylpropyl)-4-butoxymethyl-phenol,
- (\pm)-acetic acid 2-(3-diisopropylamino-1-phenylpropyl)-4-methoxymethylphenyl ester,
- (\pm)-acetic acid 2-(3-diisopropylamino-1-phenylpropyl)-4-ethoxymethylphenyl ester,
- (\pm)-2-(3-diisopropylamino-1-phenylpropyl)-4-trimethyl-silanyloxymethylphenol,
- (\pm)-diisopropyl-[3-phenyl-3-(2-trimethylsilanyloxy-5-trimethylsilanyloxymethylphenyl)-propyl]-amine,
- (\pm)-[3-(3-diisopropylamino-1-phenylpropyl)-4-trimethylsilanyloxyphenyl]-methanol,
- (\pm)-diisopropyl-[3-(5-methoxymethyl-2-trimethylsilanyloxyphenyl)-3-phenylpropylamine,

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(±)-diisopropyl-[3-(5-ethoxymethyl-2-trimethylsilyloxyphenyl)-3-phenylpropylamine,
(±)-[4-(tert-butyl-dimethylsilyloxy)-3-(3-diisopropylamino-1-phenylpropyl)-phenyl]-
methanol,
(±)-acetic acid 4-(tert-butyl-dimethylsilyloxy)-3-(3-diisopropylamino-1-phenylpropyl)-benzyl
ester,
(±)-4-(tert-butyl-dimethylsilyloxy)-3-(3-diisopropylamino-1-phenylpropyl)-phenol,
(±)-acetic acid 4-(tert-butyl-dimethylsilyloxy)-2-(3-diisopropylamino-1-phenylpropyl)-phenyl
ester,
(±)-{3-[2-(tert-butyl-dimethylsilyloxy)-5-(tert-butyl-dimethylsilyloxymethyl)-phenyl]-3-
phenylpropyl}-diisopropylamine,
(±)-[4-(tert-butyl-diphenylsilyloxy)-3-(3-diisopropylamino-1-phenylpropyl)-phenyl]-
methanol,
(±)-acetic acid 4-(tert-butyl-diphenylsilyloxymethyl)-2-(3-diisopropylamino-1-phenylpropyl)-
phenyl ester,
(±)-4-(tert-butyl-diphenylsilyloxymethyl)-2-(3-diisopropylamino-1-phenylpropyl)-phenol,
(±)-{3-[2-(tert-butyl-diphenylsilyloxy)-5-(tert-butyl-diphenylsilyloxymethyl)-phenyl]-2-
phenylpropyl}-diisopropylamine,
(±)-acetic acid 4-benzyloxy-3-(3-diisopropylamino-1-phenyl-propyl)-benzyl ester,
(±)-benzoic acid 4-benzyloxy-3-(3-diisopropylamino-1-phenyl-propyl)-benzyl ester,
(±)-isobutyric acid 4-benzyloxy-3-(3-diisopropylamino-1-phenylpropyl)-benzyl ester, and
(±)-2-(3-diisopropylamino-1-phenylpropyl)-4-(1β-D-glucurono-syloxymethyl)-phenol.

Claim 33 (new): The 3,3-Diphenylpropylamines as claimed in claim 31 selected from
carbonates and carbamates represented by the formula VII

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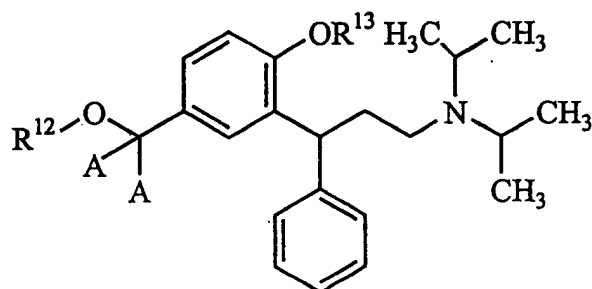
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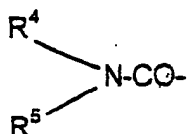
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Formula VII

wherein R^{12} and R^{13} represent a C_1-C_6 alkoxycarbonyl group or



Claim 34 (new): The 3,3-Diphenylpropylamine as claimed in claim 33 selected from
(±)-N-ethylcarbamic acid 2-(3-diisopropylamino-1-phenyl-propyl)-4-hydroxymethylphenyl ester,
(±)-N,N-dimethylcarbamic acid 2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenyl ester
(±)-N,N-diethylcarbamic acid 2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenyl ester
(±)-N-phenylcarbamic acid 2-(3-diisopropylamino-1-phenyl-propyl)-4-hydroxymethylphenyl ester,
(±)-[2-(3-Diisopropylamino-1-phenylpropyl)-4-hydroxymethyl-phenoxy carbonylamino]acetic acid ethyl ester hydrochloride,
(±)-N-ethylcarbamic acid 3-(3-diisopropylamino-1-phenylpropyl)-4-N-ethylcarbamoyloxybenzyl ester,
(±)-N,N-dimethylcarbamic acid 3-(3-diisopropylamino-1-phenylpropyl)-4-N,N-dimethylcarbamoyloxybenzyl ester,
(±)-N,N-diethylcarbamic acid 3-(3-diisopropylamino-1-phenylpropyl)-4-N,N-diethylcarbamoyloxybenzyl ester,

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(±)-N-phenylcarbamic acid 3-(3-diisopropylamino-1-phenylpropyl)-4-N-phenylcarbamoxybenzyl ester,

(±)-{4-[2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxy-methylphenoxy-carbonylamino]-butyl}-carbamic acid 2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenyl ester,

(±)-carbonic acid 2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenyl ester ethyl ester,

(±)-carbonic acid 2-(3-diisopropylamino-1-phenylpropyl)-4-hydroxymethylphenyl ester phenyl ester,

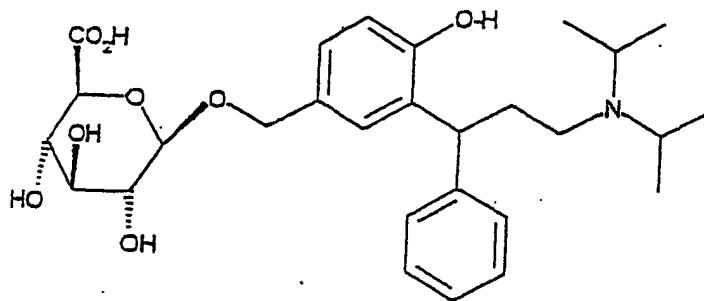
(±)-carbonic acid 2-(3-diisopropylamino-1-phenylpropyl)-4-ethoxycarbonyloxymethylphenyl ester ethyl ester, and

(±)-carbonic acid 2-(3-diisopropylamino-1-phenylpropyl)-4-phenoxy-carbonyloxymethylphenyl ester phenyl ester.

Claim 35 (new): The 3,3-Diphenylpropylamine selected from the group consisting of:

(i) (±)-Benzoic acid 2-(3-diisopropylamino-1-phenylpropyl)-4-sulphooxymethyl-phenyl ester,

(ii) (±) -2- (3-Diisopropylamino-1-phenylpropyl) -4- (1β-D-glucuronosyloxymethyl)- phenol having the formula



and

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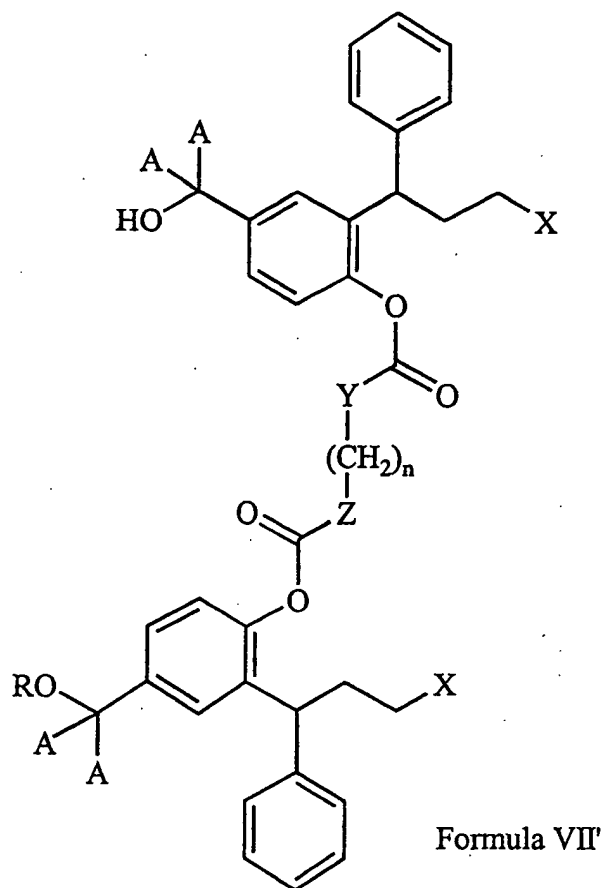
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their salts with physiologically acceptable acids, their free bases and, when the compounds are in the form of optical isomers, the racemic mixture and the individual enantiomers.

Claim 36 (new): A 3,3-Diphenylpropylamine of the formula VII':



Formula VII'

wherein R is

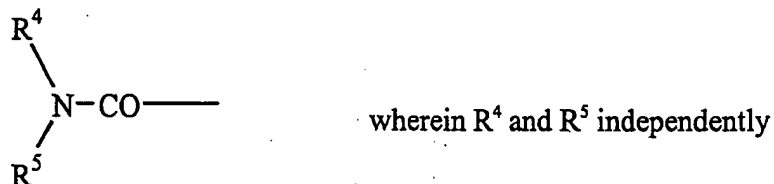
- a) C₁-C₆ alkyl, C₃-C₁₀ cycloalkyl, substituted or unsubstituted benzyl, allyl or carbohydrate;

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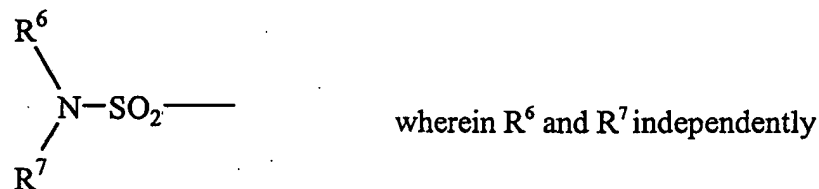
b) C₁-C₆ alkoxy carbonyl, substituted or unsubstituted aryloxy carbonyl, benzoylacyl, benzoylglycyl, a substituted or unsubstituted amino acid residue;

c)



represent hydrogen, C₁-C₆ alkyl, substituted or unsubstituted aryl, benzyl or phenoxyalkyl wherein the alkyl residue has 1 to 4 carbon atoms and wherein R⁴ and R⁵ may form a ring together with the amine nitrogen;

d)

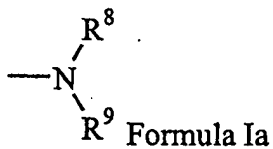


represent C₁-C₆ alkyl, substituted or unsubstituted aryl, benzyl or phenoxyalkyl wherein the alkyl residue has 1 to 6 carbon atoms;

e) an ester moiety of inorganic acids; or

f) -SiR_aR_bR_c, wherein R_a, R_b, R_c, are independently selected from C₁-C₄ alkyl or aryl, with the proviso that R' is not hydrogen, methyl or benzyl if R is hydrogen, R is not ethyl if R' is hydrogen,

X represents a tertiary amino group of formula Ia



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wherein R⁸ and R⁹ represent non-aromatic hydrocarbyl groups, which may be the same or different and which together contain at least three carbon atoms, and wherein R⁸ and R⁹ may form a ring together with the amine nitrogen,

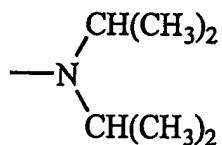
Y and Z independently represent O, S or NH,

A represents hydrogen (¹H) or deuterium (²H),

n is 0 to 12, and

their salts with physiologically acceptable acids, their free bases and, when the compounds are in the form of optical isomers, the racemic mixture and the individual enantiomers.

Claim 37 (new): The 3,3-Diphenylpropylamines as claimed in claim 36, wherein X is



Claim 38 (new): The 3,3-Diphenylpropylamine as claimed in claim 37 selected from carbonates and carbonates represented by the formula VIII:

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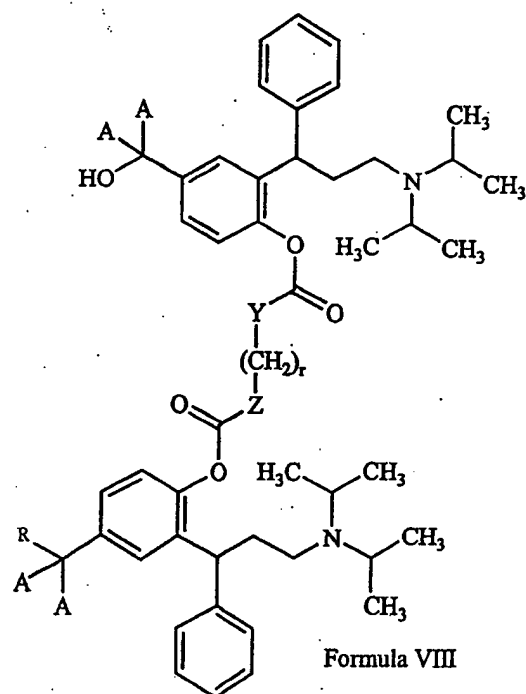
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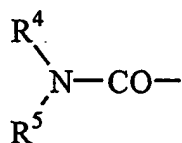
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wherein Y and Z independently represent O or NH, and

R represents a C₁-C₆ alkoxy carbonyl group or



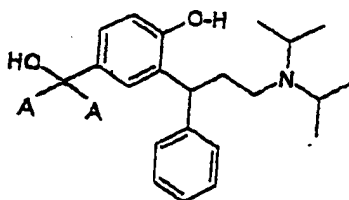
Claim 39 (new): A pharmaceutical composition comprising a 3,3-diphenylpropylamine according to any one of claims 28-38 and a pharmaceutically acceptable carrier.

Claim 40 (new): A pharmaceutical composition of claim 39 wherein the composition is a patch formulation.

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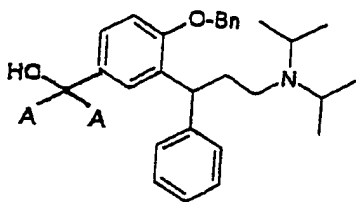
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Claim 41 (new): A process for the production of ethers according to claim 31, wherein R¹¹ is hydrogen, which comprises reacting a compound of the formula

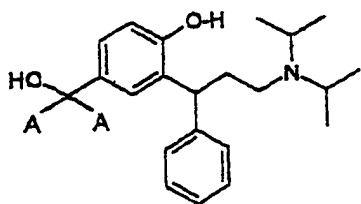


with an alcohol R¹⁰-OH in the presence of an esterification catalyst.

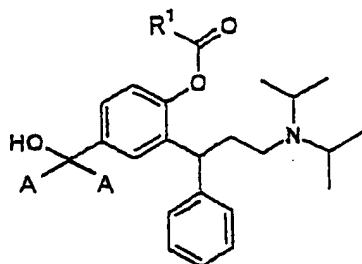
Claim 42 (new): A process for the preparation of ethers according to claim 31, which comprises acid or base treatment, in the presence of suitable hydroxy reagents, of a compound selected from



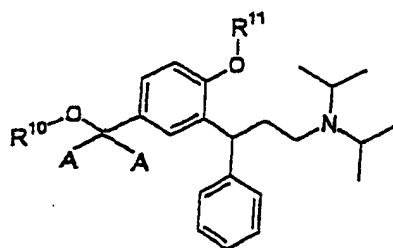
(a)



(b)

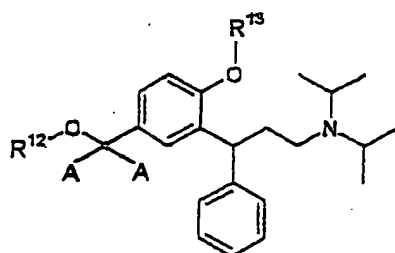


(c) Formula II



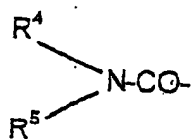
(d) Formula VI

wherein R¹⁰ is hydrogen,



(e) Formula VII

wherein R¹² is hydrogen and R¹³ represents a C₁-C₆ alkoxy carbonyl group or



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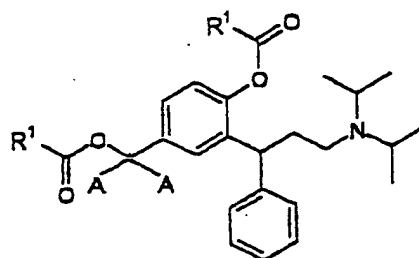
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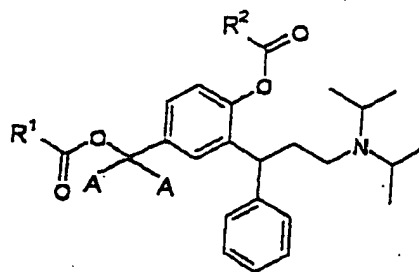
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wherein R^4 and R^5 independently represent hydrogen, C_1 - C_6 alkyl, substituted or unsubstituted aryl, benzyl or phenoxyalkyl wherein the alkyl residue has 1 to 4 carbon atoms or R^4 and R^5 form a ring together with the amine nitrogen, and

(f) benzylic acylates selected from

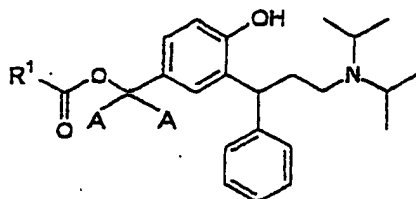


Formula III



Formula IV

and



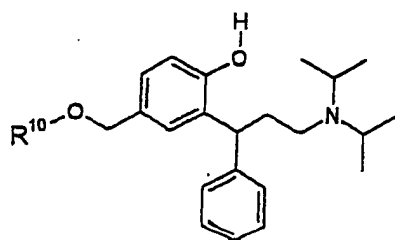
Formula V

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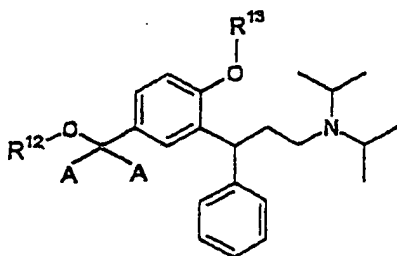
wherein R^1 is hydrogen, C_1 - C_6 alkyl or phenyl, and R^2 represents hydrogen, C_1 - C_6 alkyl or phenyl, with the proviso that R^1 and R^2 are not identical.

Claim 43 (new): A process for the preparation of ethers of formula VI according to claim 31, which comprises treating a compound of the formula



with an alkylating agent selected from alkyl halides, alkyl sulphates and alkyl triflates, said alkyl group having 1 to 6 carbon atoms.

Claim 44 (new): A process for the preparation of carbonates and carbamates as claimed in claim 33, represented by formula VII:

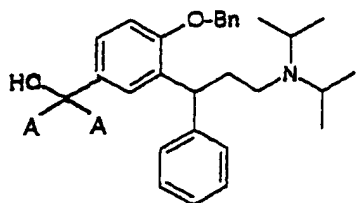


Formula VII

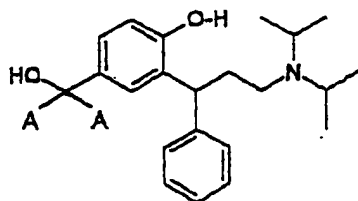
which comprises reacting a compound selected from the group consisting of
(a)

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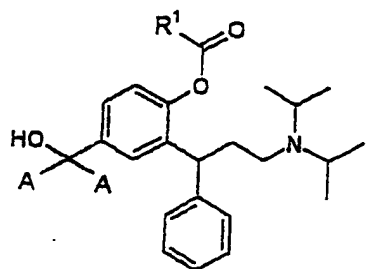
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(b)

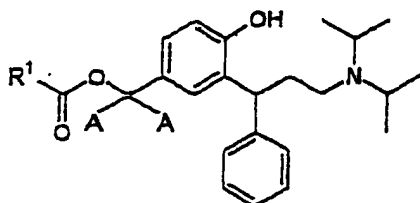


(c)



Formula II

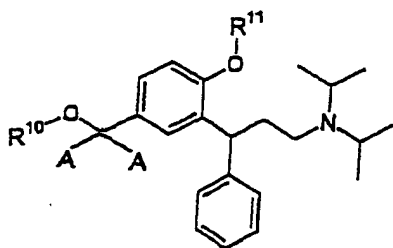
(d)



Formula V

and

(e)



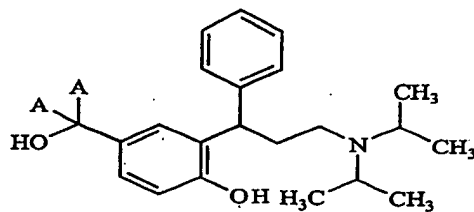
Formula VI

wherein R^1 represents hydrogen, C_1 - C_6 alkyl or phenyl, n is 0 to 12, Bn is benzyl, one of R^{10} or R^{11} is hydrogen and the other one is C_1 - C_6 alkyl, benzyl, $-\text{SiR}_a\text{R}_b\text{R}_c$, C_1 - C_6 alkylcarbonyl or benzoyl, wherein R_a , R_b , R_c are independently C_1 - C_4 alkyl or aryl, with activated carbonyl compounds or carbonyl precursor reagents selected from haloformates, ketenes, activated esters, mixed anhydrides of organic or inorganic acids, isocyanates and isothiocyanates.

Claim 45 (new): A process for the preparation of carbonates and carbamates according to claim 33 which comprises reacting a compound of formula

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with activated carbonyl compounds or carbonyl precursor reagents selected from haloformates, isocyanates and isothiocyanates.

Claim 46 (new): A method of antagonizing a muscarinic receptor, the method comprising contacting the receptor with a compound according to any one of claims 28-38.

Claim 47 (new): A method of treating a disease in a mammal that is amenable to treatment by antagonizing muscarinic receptors in the mammal, the method comprising administering an amount of a composition according to claim 39 effective to diminish or eliminate symptoms of the disease.

Claim 48 (new): The method according to claim 47 wherein the disease is urinary incontinence.

Claim 49 (new): The method according to claim 48 wherein the mammal is a human.